

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

The Office Action identifies claims 1-4, 6, 7, 13, 18, 28, 37, 49 and 51 as currently being prosecuted. This listing of the claims is, however, incorrect. Applicants direct the Examiner's attention to their response to the Restriction Requirement filed on February 21, 2008 indicating the election of claims 1-4, 6-13, 18-32, 37 and 49-51 as those which read on elected group Group IV, with claims 1-4, 6, 7, 11-13, 18, 25, 26, 28, 37, 49 and 51 belonging to the elected species. See pages 11 and 12 of the response. Applicants respectfully request the Examiner to correct this mistake. A detailed listing of the claims along with their appropriate status identifiers is provided along with this response for the Examiner's convenience.

Applicants have amended claims 1-4, 28 and 37 to overcome the §112 rejections. Claims 1-4 and 37 have been amended to recite "a composition comprising a carbon-bound diazeniumdiolate...". Support for this amendment can be found throughout the specification and especially in paragraphs 13 and 20 of Published Application No. US 2007/0286840. Further, claim 13 has been cancelled and the subject matter of claim 13 has been introduced into amended claim 3. The amendments introduce no new subject matter which would require a new search. Claims 1-4, 6, 7, 11-12, 18, 25-26, 28, 37, 49 and 51 are currently pending in this application, with claims 1, 2, 3, 4 and 37 being independent claims.

***The Specification Provides Written Description Support for the Claimed Invention:***

Claims 1-4, 6, 7, 13, 18, 28, 37, 49 and 51 are rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. Applicants respectfully traverse.

Claim 13 has been cancelled rendering the rejection of claim 13 moot.

A. The Office objects that the term "phenyl-containing polymers" describes a broad genus and claims 1, 2, 6, 7, 13, 18, 28 and 37 fail to recite any structural features

common to the members of such a genus. The written description requirement requires that the patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. See MPEP §2163. The MPEP further states that possession of the claimed invention is shown by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

The instant specification contains a complete description of the claimed invention. The specification and working examples support the inventive compositions and the Examiner's remarks to the contrary are unsupported.

Applicants state that the term "phenyl-containing polymers" would be easily understood by one of ordinary skill in general chemistry to mean a polymer of covalently linked phenyl groups. While the term alone sufficiently describes the polymer, Applicants state that the specification provides further support for phenyl-containing polymers used in the inventive compositions. For example, Formulas 2 and 3 pictorially depict the structure of a phenyl-containing polymer. See page 2, right column of the Published Application No. 2007/0286840. The specification also provides a generic formula for such a polymer (Formula 1). As described in the specification the phenyl group may be pendant from the polymer backbone (Formula 2) or it is a part of the polymer backbone (Formula 3). *Id.* The specification lists exemplars of phenyl containing polymers and also provides a description for synthesizing polymers containing the pendant phenyl group as well as polymers in which the phenyl group is part of the polymeric backbone. See ¶¶ 24, 29-31, 45 and 47-48 of the Published Application No. 2007/0286840. Moreover, the working examples provide further support for compositions having phenyl-containing polymers. See example 1-8.

In view of the above remarks Applicants respectfully request reconsideration and withdrawal of this rejection.

**B.** The Office states that the specification fails to disclose specific “nitric oxide releasing polymers” and claims 49 and 51 fail to recite structural features common to the members of that genus. Applicants respectfully traverse.

The present specification provides analytical data for NO-release using a cyano-modified chloromethyl styrene polymer as well as an ethoxy-modified chloromethyl styrene polymer. See paragraphs 14, 15 and Figures 1 and 2. The specification further describes the structural features that can be altered to modulate the degree and rate of NO release from the NO-releasing polymers. For example, the specification teaches altering the NO-release profile by altering the electronic properties of  $R^1$  in Formula 1. The present specification also describes chloromethylated polystyrene cross-linked with divinylbenzene as another exemplar of an NO-releasing polymer having two different types of NO-releasing moieties, (e.g.  $R^{1a}$  and  $R^{1b}$ ). See paragraph 50 and Scheme 3.

Furthermore, Example 12 compares the ability of three NO-releasing polymers to inhibit agonist induced platelet aggregation. As described in the specification the thioethyl NO-releasing polymer is better at inhibiting platelet aggregation than the ethoxy or cyano substituted polymers.

Contrary to the Examiner’s assertion, the specification describes specific NO-releasing polymers and as mentioned above, provides ample guidance for the structural features of the NO-releasing polymers. Thus, the specification conveys the possession of the inventive compositions at the time of filing of this application. The written description rejection is improper and Applicants respectfully request reconsideration and withdrawal of this rejection.

**C.** The Office states that the term “means for” covalently linking in claim 37 is indistinct and fails to reasonably convey to a skilled artisan that the Applicant was in possession of a representative number of species within the genus. Applicants respectfully traverse and state that the term “means for” does not render claim 37 indefinite.

However, to further prosecution and without acquiescing to the merits of the rejection, Applicants have amended claim 37 to recite a system for localized release of nitric oxide to a

target site comprising a phenyl-containing polymer and a carbon-bound diazeniumdiolate nitric oxide donor molecule that is not an imidate or thioimidate. Amended claim 37 further recites that the nitric oxide donor molecule is linked to the polymer to produce a carbon-bound diazeniumdiolate moiety.

This amendment overcomes the indefiniteness rejection, therefore, Applicants respectfully request the Examiner to withdraw the same.

***The Claims Point out and Distinctly Claim the Inventive Subject Matter:***

Claims 1-4, 6, 7, 13, 18, 28, 37, 49 and 51 are rejected under 35 USC §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Claim 13 has been cancelled rendering the rejection of claim 13 moot.

The Examiner states that R<sup>1</sup> is defined in terms of “what it is not” which renders claim 3 indefinite. Applicants have amended claim 3 to recite R<sup>1</sup> in Markush group terms. Thus, the rejection is moot in light of this amendment.

The Examiner states that the term “terminal oxygen” in claim 3 lacks sufficient antecedent basis. Applicants have amended claim 3 to provide antecedent basis and request the Examiner to withdraw the rejection.

Claim 28 has been objected to by the Examiner as being indefinite for reciting both a broad and a narrow recitation. Applicants have amended the claim to overcome this rejection. Furthermore, amended claim 28 does not recite the term “including” objected to by the Examiner. The present amendments overcome the Examiner’s objections, thus, the Examiner is respectfully requested to withdraw the same.

The Examiner also objects to the term “carbon-based” as being indefinite. When read in the context of the claim, the term carbon-based would be understood by a skilled artisan to mean a diazeniumdiolate moiety bound to a carbon atom as shown in Formula 1. However, to further prosecution Applicants have amended the claims to recite a composition

comprising "a carbon-bound diazeniumdiolate compound" which overcomes the indefiniteness objection. See paragraphs 13 and 20 of Published Application No. US 2007/0286840. Withdrawal of the indefiniteness objection is therefore respectfully requested in view of this amendment.

***Non-obviousness of the Claims in view of the cited References:***

I. Claims 1 and 2 are rejected as being unpatentable over Cafferata (U.S. Patent Publication No. 2003/0083739) in view of Arnold *et al.*, Nitric Oxide, 2002 (Arnold (A)). Applicants respectfully traverse.

Claim 13 has been cancelled rendering the rejection of claim 13 moot.

i. Current Obviousness Standard

The Supreme Court recently reaffirmed the Graham factors for determining obviousness in *KSR Int'l Co. v. Teleflex Inc.* (No. 04-1350) (U.S., April 30, 2007). The Graham factors, as outlined by the Supreme Court in *Graham et al. v. John Deere Co. of Kansas City et al.*, 383 U.S. 1 (1966), are: 1) determining the scope and contents of the prior art; 2) ascertaining the differences between the claimed invention and the prior art; 3) resolving the level of ordinary skill in the pertinent art; and 4) evaluating evidence of secondary consideration. The Supreme Court recognized that a showing of "teaching, suggestion, or motivation" to combine the prior art to meet the claimed subject matter could provide a helpful insight in determining whether the claimed subject matter is obvious under 35 U.S.C. § 103(a), and held that the proper inquiry for determining obviousness is whether the improvement is more than the predictable use of prior art elements according to their established functions. The Court noted that it is "important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the [prior art] elements" in the manner claimed, and specifically stated:

Often, it will be necessary . . . to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was ***an apparent reason to combine the known elements in the fashion***

***claimed*** by the patent at issue. To facilitate review, this analysis should be made explicit.

*KSR Int'l Co. v. Teleflex Inc.*, slip op. at 14 (emphasis added). Applicant respectfully asserts that the Office has not met its burden.

ii. Cafferata in view of Arnold

The Examiner has acknowledged that Cafferata does not teach or suggest a composition having a carbon diazeniumdiolate compound attached to a phenyl containing polymer. In fact, Cafferata teaches a system and a method for treating vascular restenosis that combines **two disparate** drug delivery systems that act synergistically for maximum therapeutic effect. Specifically, Cafferata's system combines the systemic delivery of a non-toxic, sub-threshold dose of a drug with a targeted delivery of the second drug using catheter mediated stent placement.

To remedy the deficiencies in Cafferata, the Examiner relies on Arnold. Arnold is cited to teach a carbon-bound diazeniumdiolate compound and the Examiner is of the opinion that the combination of Arnold (A) and Cafferata render the inventive composition obvious. Applicants respectfully traverse.

The focus of the Arnold publication is on the mechanism for NO production by a carbon-bound diazeniumdiolate compound. Specifically, Arnold (A) discloses the kinetics for the release of NO from *bis*-diazeniumdiolate under acidic conditions. Moreover, Arnold does not teach or even suggest attaching the disclosed carbon-bound diazeniumdiolate to a phenyl-containing polymer, much less teach a composition of a diazeniumdiolate compound as recited by amended claim 1.

The inventive composition, in contrast, comprises a carbon diazeniumdiolate compound that is attached to at least one phenyl-containing polymer. Neither Cafferata nor Arnold (A) disclose the inventive combination independently and Arnold (A) does not remedy the deficiencies in Cafferata's composition. Thus, contrary to the Examiner's suggestion, combining the teachings of Arnold and Cafferata would not allow a skilled Artisan to arrive at the claimed composition because Cafferata's composition requires a two drug system.

In view of the remarks made above, Applicants state that the inventive compositions of claims 1 and 2 are not obvious over the combined teachings of Cafferata and Arnold (A). Applicants respectfully request the Examiner to withdraw this rejection.

II. Claims 3, 4, 6, 7, 13, 18, 28, 37, 49 and 51 are rejected under 35 USC §103(a), as being unpatentable over Cafferata (U.S. Patent Publication No. 2003/0083739) in view of Arnold *et al.*, Org. Letters, 2002 (Arnold (B)) and further in view of Arnold *et al.*, Nitric Oxide, 2002 (Arnold (A)). Applicants respectfully traverse.

Claim 13 has been cancelled rendering the rejection of claim 13 moot.

Claims 6, 7, 28, 49 and 51 depend on independent claim 1 which is not rejected in this section of the Office Action. Thus, the rejection of these claims is improper. However, as stated above, independent claim 1 is not obvious over the combination of Cafferata and (A). As disclosed below, (B) does not remedy the deficiencies of Cafferata's composition. Therefore, claims 6, 7, 28, 49 and 51 are patentable over the combination of the three cited references.

The Examiner has acknowledged that Cafferata does not teach a NO-releasing carbon diazeniumdiolate compound that is attached to at least one phenyl containing polymer. The Examiner further acknowledges that the NO-releasing diazeniumdiolate compound taught by Cafferata does not have a cyano group and lacks sodium as the counteranion. As mentioned above, Cafferata does not teach the inventive composition because Cafferata discloses a two drug system.

To remedy the deficiencies in Cafferata the Examiner cites Arnold (B), stating that the carbon diazeniumdiolate compound taught by this reference reads on the compound recited in claim 3. This assertion, however, is improper. The carbon diazeniumdiolate compound (1) disclosed in (B) is a methane trisdiazeniumdiolate. See abstract and Scheme 1. It has three N<sub>2</sub>O<sub>2</sub> attached to a carbon atom. In contrast, the compound represented by the formula in claim 3 has two N<sub>2</sub>O<sub>2</sub> groups and a cyano group as the third functional group on the carbon atom. Thus, contrary to the Examiner's assertion, one of ordinary skill would not arrive at the

inventive composition by attaching the methane trisdiazoniumdiolate of (B) to the phenyl containing polymer of Cafferata.

The Examiner is also of the opinion that the composition obtained by combining the teachings of Cafferata with (B) when coated on to a medical device would read on the medical device of pending claims 49 and 51. Because, the combination of Cafferata and (B) would fail to result in the inventive composition, coating such a composition on to a medical device as stated by the Examiner would not render claims 49 and 51 unpatentable.

Independent claims 3, 4 and 37 are therefore patentable over the combination of Cafferata, Arnold (A) and Arnold (B).

Claim 18 depends on patentable claim 3 and incorporates all its limitations. Thus, the dependent claims are patentable over the cited references for at least the same reasons mentioned above for overcoming the rejection of claim 3.

Applicants state that all claims are now in condition for allowance and respectfully request the Examiner to reconsider and withdraw the rejections.



CONCLUSION

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing or a credit card payment form being unsigned, providing incorrect information resulting in a rejected credit card transaction, or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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FOLEY & LARDNER LLP  
Customer Number: 22428  
Telephone: (202) 295-4620  
Facsimile: (202) 672-5399

By Richard C. Peet

Richard C. Peet  
Attorney for Applicant  
Registration No. 35,792